REMARKS

Claim objections

Applicant thanks the Examiner for noting that the subject matter of claim 20 is allowable. Applicant has not rewritten the subject matter of claim 20 as an independent claim but reserves the right to do so in a future amendment.

Rejections under 35 U.S.C. § 112

Claim 30 stands rejected under 35 U.S.C. 112. Applicant has removed the language objected to by the Examiner. Applicant submits that the claims meet all the requirements of 35 U.S.C. 112.

Rejections under 35 U.S.C. § 103

Claims 1-3, 5-8, 19, 22-24, and 27-40 stand rejected under 35 U.S.C. 103 as being obvious in view of Holmes A in view of Hubbell. Applicant respectfully disagrees.

With respect to claim 1, Applicant submits that the combination of Holmes A and Hubbell fails to result in or render obvious the invention. Holmes A discloses the formation of membranes from amphiphilic peptides having alternating hydrophobic and hydrophilic peptides. The membranes form spontaneously in the presence of metal cations (see column 8, lines 5-10). Cells are not encapsulated within individual membranes, in contrast to amended claim 1 ("said cells being present *within* said macroscopic scaffold..."). Rather, cells may be layered *between* membranes, as disclosed by column 12, lines 1-9. As noted by the Examiner, the cells are larger than pores within the membranes (Office Action dated June 22, 2005, page 3, lines 21-22). If the cells are larger than the pores within the membrane, they cannot themselves be within the membrane. Rather, they are contained between the membrane layers. The use of stacked membranes, as disclosed at column 12, line 3, enables the skilled artisan to overcome the "surface-to-volume limitation" (column 12, line 1) of tissue culture dishes. The small pore size of the membranes prevents cell migration between layers. It is clear from the repeated discussion of culturing cells *on* the membranes of Holmes A (see column 11, lines 32-35, describing cell adhesion to surfaces, column 11, lines 39-40, describing cell adherence to EAK16 membranes, column 11, line 60, describing cell monolayers, and column 12, line 10, describing cell growth on the disclosed biopolymers) that the cells are not present within the membrane, whether or not

it is termed a scaffold and despite the three dimensional structure revealed by SEM (see column 3, line 66- column 4-line 3).

Hubbell discloses the encapsulation of cells within hydrogels. Hydrogels are defined as "a substance formed when an organic polymer (natural or synthetic) is crosslinked via covalent, ionic, or hydrogen bonds to create a three-dimensional open-lattice structure which entraps water molecules to form a gel" (column 7, lines 37-41). The open-lattice structure is isotropic and is formed by randomly oriented polymer chains that are each cross-linked to multiple chains.

Applicant submits that there is no indication in Holmes A of how to encapsulate cells within membranes, nor is there any teaching in Hubbell that suggests a suitable procedure or that cells might be successfully encapsulated within the beta-sheet peptide structure. The hydrogels of Hubbell are formed by a different chemical mechanism than the peptide membranes of Holmes. A. The hydrogels are formed by cross-linking. The definition provided by Hubbell indicates that the polymer precursors can form the hydrogel in the absence of cells, and Hubbell provides a disclosure of cells being trapped within hydrogels during the cross-linking process. In contrast, three different types of interactions, none involving the cross-linking of polymer chains, contribute to the self-assembly of the anisotropic peptide membranes of Holmes A. In contrast, as discussed in column 5, lines 10-22 of Holmes A, individual peptide chains interact with each other through hydrogen bonding to form beta-sheets (Figure 5B, y-axis). The beta-sheet is stabilized in the x-direction by mechanical staggering of the chains. In the z-direction, the layers of beta-sheets are stabilized by ionic and hydrophobic interactions. Hubbell fails to disclose that a single material may form a three-dimensional structure through a combination of multiple types of interactions. Indeed, mechanical interlocking is not disclosed as a mechanism for the formation of hydrogels in Hubbell. There is no indication in either Holmes A or Hubbell that the presence of cells during peptide self-assembly will not disrupt one or more of these interactions and prevent organized self-assembly. Hubbell further does not teach how to combine cells and any polymer in a manner in which the polymer will self-assemble in an ordered structure rather than forming a randomly ordered, isotropic hydrogel.

With respect to claims 36-39, Applicant submits that neither Holmes A nor Hubbell discloses the use of a solution of peptides containing a carbohydrate or glycerol, as recited in the amended claims. The amendments are supported by the specification at page 2, lines 20-24. As noted above, Holmes A fails to disclose combining cells with a solution of peptides, and Hubbell

discloses that the preferred solution for the combination of cells and a polymer is a potassium phosphate solution (column 10, line 32). Such a solution would cause the peptides of claims 36-39 to self-assemble, contrary to the recitations of the claims that the peptide does not self-assemble until addition of an electrolyte.

Claim 4 stands rejected under 35 U.S.C. 103 as being obvious in view of Holmes B and Hubbell. Applicant submits that Holmes B does not remedy the failure of Holmes A and Hubbell to disclose or render obvious the invention of claim 1, from which claim 4 depends.

Applicant submits that 1-8, 19, 20, 22, 22-24, and 27-40 are patentable in view of Holmes A, Holmes B, and Hubbell, whether considered separately or in any combination.

A petition for extension of time, a request for continued examination, and the appropriate fees are enclosed. Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully submitted,

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